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PRINCIPAL INVESTIGATOR: M. Ricardo Richardson, Ph.D.

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14. ABSTRACT
The NCCU/BBRI-Duke/Urology Partnership in Prostate Cancer Research was developed to promote Collaborative Training, Research, and Community Dialogue and Outreach among scientists from NCCU and Duke. During the first funding period, NCCU scientists, with the expertise of their Duke partners, have started five collaborative pilot projects. These projects have provided needed training for NCCU scientists in the development and approval of IRB protocols for research involving human subjects, and access to key core facilities and libraries at Duke. Some reagents important to the success of the projects have been developed including a mouse model of prostate cancer deficient in ••arrestin 2 (TRAMP-˜arr2-/-) or 5-Lox (TRAMP-Alox5-/). Several prostate cancer cell lines have also been adapted to the principal investigators laboratories for in vitro studies. Our collaboration has also led to the submission of three grant proposals: one to the USAMRMC and two to the National Institute of Health. The USARMC proposal entitled: "Association of the UGT2B17 Gene Deletion Polymorphism and the Incidence of Ovarian Cancer and Ethnicity" and the Export project entitled "Roles of Inflammation and Androgen Metabolism in Prostate Cancer Disparity" have been funded. The U54 application in partnership with UNC-Lineberger and Duke Comprehensive Cancer Centers entitled "NCCU-DCCC-LCCC Partnership In Cancer Research" is under revision.

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Introduction:

Prostate cancer is the most common cancer in men resulting in the loss of 30,000 lives per year in the United States. An estimated 218,890 new cases were diagnosed in 2007 (1, 2). African Americans are more likely to develop prostate cancer than any other racial or ethnic groups. Although the survival rates for cancer has improved, for people of African descent, survival rates for prostate cancer and other cancers are dismally worse compared to Caucasians. African Americans still have higher risk and poorer clinical outcomes than any other ethnic groups (3). Could it be possible the poorer health outcomes for African Americans and other minority groups result from their lack of representation in scientific research? Since it is well recognized that minorities are more likely to trust and cooperate with minority scientists in their community to address minority related health issues, building a diverse pool of scientists and clinical investigators is critical to reduce health disparities. The long-term goal of the NCCU/BBRI-Duke/Urology Partnership is to develop innovative approaches for prevention, detection, and treatment of prostate cancer, through research, training and collaboration between these two institutions. Community outreach through one of the leading Historically Black Colleges and Universities (HBCU) in this country will eventually help address the issue of health disparity in Durham and the surrounding area of North Carolina, where there is a large population of African Americans.

Body:

Task #1: Create the Prostate Cancer Disparity Research and Training Center (PCDRT) and develop plan for training.

a) We have created the Collaborative Prostate Center and developed a plan for **Training**, **Research**, and **Community Dialogue and Outreach** and established our program advisory committee. Our first meeting was held at the JLC-BBRI and was attended by the Principal Investigators and the research teams from both Duke and NCCU.

b) Ms. Sacajawea Gray replaced Ms. Romelia Perez as Administrative Assistant for the Cancer Research Program. A Program Steering Committee meeting was held in the auditorium of the JLC-Biomedical Biotechnology Research Institute of NCCU on May 22, 2008. The Principal Investigators (PI) and Co-PI presented the hypotheses and aims of their project followed by a discussion.

c) The cancer group met weekly (Mondays at 9 a.m.) to discuss the projects and relevant manuscripts in prostate cancer. Bi-weekly meeting were also conducted at the Duke/VA with our Duke collaborators to discuss samples accrual, IRB approval and other issues. In addition, the group has a monthly progress report meeting, held the last Monday of each month, in which data from a project is presented to the rest of the group, followed by a discussion.

d) Scientists from NCCU have attended the Duke Symposium in Prostate Cancer held in February 2008 at the Duke Comprehensive Cancer Center.

e) Drs. Richardson, Chen and Grant in collaboration with our Duke Collaborators wrote a full proposal entitled: “Roles of Inflammation and Androgen Metabolism in Prostate Cancer Disparity” that submitted in our EXPORT center grant. This proposal has been funded by National Center on Minority Health and Health Disparity (NCMHD). Dr. Grant and Dr.

Schildkraut teamed up to write a training proposal for Dr. Grant entitled: “Association of the UGT2B17 Gene Deletion Polymorphism and the Incidence of Ovarian Cancer and Ethnicity”. This proposal has been funded by the USAMRMC and works have already began. In collaboration with our partners at Duke Comprehensive Cancer Center (DCCC) and UNC Lineberger Comprehensive Cancer Center (LCCC) we have submitted a U54 grant application (U54CA137837) to the National Cancer Institute entitled “NCCU-DCCC-LCCC Partnership in Cancer Research”. This three-way partnership has a combined budget of 14.9 million dollars.

Task #2: Develop a core facility for the Collection of clinical samples and data.

a) Ms. Kelly Anderson has been recruited in February 2008 as a Research Associate to assist the Duke team in the collection of clinical samples.

b) The NCCU team of investigators led by Dr. Grant and the Duke investigators by Dr. Freeland meet weekly at the Duke VA to discuss the training of Ms. Anderson, the modifications of the IRB protocol and questionnaire, and the logistics concerning the future accrual and distribution of samples when the final IRB is approved. The Research Associate was supposed to be at Duke 50% of the time and, as a consequence, 50% salary support was requested in the original proposal. The task, however, requires Ms. Anderson to be on site 100% of the time. We have requested a revised budget to reflect this need.

c-e) Subject recruitment, data collection of enrolled patients, processing and distribution of samples to NCCU scientists are awaiting final IRB approval from the DOD.

Task #3: Develop 5 pilot studies focusing in the molecular, genetic socio-cultural aspects of prostate cancer incidence and disparities.

a) A NCCU approved IACUC protocol was submitted to the Department of Defense. This protocol includes several mouse strains including the TRAMP model that is being crossbred with the β-arrestin 2 knockout to generate the TRAMP-βarr2-/- model.

b) The research team of NCCU/BBRI scientists in collaboration with scientists and clinicians from Duke/Urology Department has developed a Collaborative Research Center in Prostate Cancer to promote independent, competitive research and training programs. Five independent studies focusing on the molecular, genetic and socio-cultural aspects of prostate cancer disparities were developed. Below is the progress of each project along with the significance and future directions.

Pilot Project #1: The UGT2B Gene Polymorphisms and its Association with Prostate Cancer Disparity

Investigator: Delores Grant, Ph.D. NCCU

Collaborators: Cathrine Hoyo, PhD, Stephen Freedland, MD, Joellen Schildkraut, PhD, Philip Febbo, MD, Duke/Urology

A. Specific Aims

1) Determine whether there is an association between the *UGT2B17* deletion and *UGT2B15*^{D85Y} genotype in genomic DNA samples and prostate cancer risk using a case control study in African and Caucasian populations
2) Compare expression levels of the *UGT2B17* gene in RNA samples from the prostate cancer cases and controls and determine whether these also vary by race;
3) Quantitate serum glucuronides of testosterone and testosterone metabolites among controls to determine association with 0, 1, or 2 copies of *UGT2B17* and;
4) Compare expression levels of the *UGT2B17* gene in prostate cancer tissue and normal margins utilizing tissue microdissection and immunohistochemistry

B. Studies and Results

In the direction of accomplishing these Aims we have designed a hospital based case control study. Participants will be recruited from the Veterans Administration Medical Center (VAMC) in Durham, including the number of subjects (cases and controls) that can be accrued form the facility, given patient volume. We have identified inclusion and exclusion criteria. In addition, we have recruited and trained a research assistant, Ms. Kelly Anderson, in collecting peripheral blood, administering the 10-page questionnaire, entering data into an electronic data base, and preparing accrual reports. In preparation for starting the study, the research assistant has been trained to amend Duke and the VA Institutional Review Board (IRB) to the ongoing case-control study to ensure that the Specific Aims are met. Because investigators on the study are Duke employees and data are collected from the VAMC, preparing IRB requests for approval have involved preparing three separate requests; one for the VAMC, a separate IRB request for Duke University and a third for the United States Army Medical Research and Material Command's (USAMRMC) Office of Research Protection (ORP), Human Research Protection Office (HRPO). We are currently addressing changes outlined in the Protocol Addendum to Dr. Stephen Freedland's "A Comparative Study of Risk Factors for Men with and without Prostate Cancer", HRPO Log Number A-14291.1 and the Memorandum for Record (MCMR-ZB-PH (70-1n1)). We have previously submitted amendments to Dr. Freedland's protocol in March 2008 which required further changes. This has ultimately delayed the start of our study. We plan to begin accrual in the next three months.

C. Significance

Successfully addressing the Aims outlined above will enhance our knowledge of prostate cancer by identifying a combination of biomarkers that could be used in conjunction with the PSA to improve our prediction of aggressive vs. non-aggressive prostate cancer at the early stage. Questionnaire data together with specimens collected using this funding will provide a resource for NCCU to explore additional hypotheses at a future date, thus enable additional studies to be funded.

D. Plans

During the next funding cycle after approval from ORP and HRPO we will begin to recruit subjects for this study. An amended protocol will be submitted to ORP and HRPO by June 20, 2008. We

have recruited an NCCU Master of Science graduate student, Ms. Tiffany Anderson, who will be trained and co-mentored by Drs. Freedland, Hoyo, and Grant during the next cycle. We will also conduct laboratory and statistical analyses using data collected. If findings are promising, we will apply for additional funding to investigate this hypothesis in more samples.

E. Publications

No publications

F. Project-Generated Resources

Samples and questionnaire data will be generated and kept as a common resource for NCCU faculty. No other resources were generated

Pilot Project #2: Role of β-arrestins in prostate cancer development and its contribution to Prostate Cancer Disparity

Investigator: M. Ricardo Richardson, PhD. NCCU/BBRI**.**
Collaborators: Judd Moul, M.D., Duke/Urology

A. Specific Aims

1) To determine whether the level of expression of βarr-1 and/or βarr-2 are elevated in prostatic tissues from African American Men (AAM) relative to Caucasians American men (CAM).
2) To develop the TRAMP mouse model of prostate cancer in mice deficient in either βarr-1 or βarr-**2**

B. Studies and Results

1. Our studies using both RT-PCR (Fig 1-A) and Western blotting (Fig 1-B) have shown that expression of βarr-1, but not βarr-**2**, is markedly increased in prostatic cell lines from both AAM (E006AA) and CAM (PC3) compared to control prostate cell lines (RWPE1 and RWPE2). With our collaborators at Duke/VA an IRB has been developed and is currently being revised to be submitted to the USARM for final approval. We are waiting for the final approval of the IRB to start accruing prostatic tissue samples from AAM and CAM at the Duke VA hospital with different, level of tumor aggressiveness. These samples will be used to further confirm these results and determine whether overexpression of βarr-1 is associated with tumor aggressively

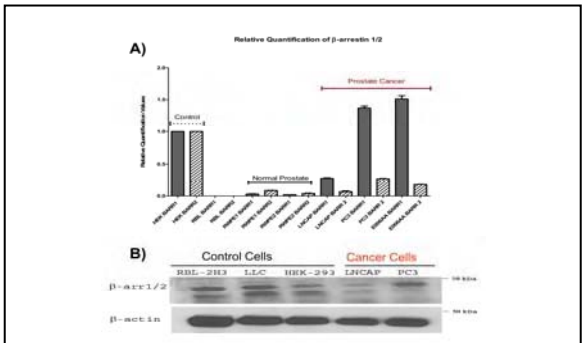


Figure 1. β-arrestin Expression in Prostate Cancer cells. A) Relative quantification of β-arrestin mRNA expression levels in prostate cell lines. Quantities of β-arrestin 1 and 2 mRNA levels were determined in each sample using the relative quantification method of real-time PCR. Messenger RNA level of β-arrestin was measured in each sample relative to levels expressed in HEK-293 cells and normalized to the measured values of endogenous levels of ribosomal RNA 18s. Values represent means ±SEM.
B) Expression level of β-arrestin 1/2 in prostate cells. Western blot analysis was performed to measure the expression level of β-arrestin 1/2 in prostate cell lines. Cells were lysed in RIPA buffer, and a total of 20 g of protein for each lane was loaded onto an SDS-polyacrylamide gel. The membrane was blotted against β-arrestin 1/2 antibody.

2. Consistent with our plan, we have also generated a mouse model of prostate cancer deficient in βarr-2. To that end, the Transgenic Adenocarcinoma (TRAMP) mouse model (C57BL/6 strain) was crossbred with βarr2$^{-/-}$ model that is also of C57BL/6 strain (Fig 2A). Male TRAMP mice uniformly and spontaneously develop autochthonous

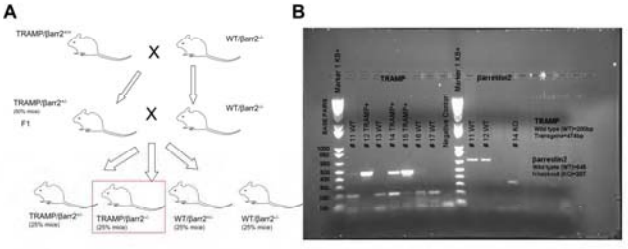


Figure 2: A) Schematic representation of coss-breeding of TRAMP positive C57BL/6 mice with βarr2$^{-/-}$ animals. F1 generation was backcrossed with βarr-2$^{-/-}$ to obtain the TRAMP-βarr2$^{-/-}$ strain. B) Genotyping results of mice from F2 generation. #14 is a representative of a TRAMP-βarr2$^{-/-}$ mouse.

prostate tumor following the onset of puberty. Male TRAMP-βarr2$^{-/-}$ (Fig 2B, animal #14) along with control TRAMP is being followed for the development of prostate tumor that usually occur between 25 to 40 weeks. Thus far, up to 30 weeks, no significant difference in tumor size has been observed between the two groups. We are currently waiting for the final approval of our ACURO protocol to breed the TRAMP-βarr2$^{-/-}$ mice with βarr2$^{-/-}$ knockout for further experiment.

C. Significance

This project is specifically designed to address one significant issue in health disparity of prostate cancer, why African American men have a higher risk of developing prostate cancer and poorer clinical outcome than Caucasian American men.

D. Plans

1. To continue the cell line experiments and determine whether expression of βarrestin-2 correlate with tumor aggressiveness.
2. To obtain IRB approval and collect prostatic tissues from human subjects.
3. To correlate the in vitro data with tumor growth and metastasis in vivo using the TRAMP-βarr2$^{-/}$ mouse model.

E. Human Subjects: Protocol under revision

F. Vertebrate Animals: No change

G. Publication: NA

Pilot Project #3: Role of 5-Lipoxygenase in Clinical Outcome of African American and Caucasian Prostate Cancer Patients

Investigator: Xiaoxin Chen, MD, PhD. NCCU/BBRI**.**
Collaborator: Leon Sun, MD, Duke/Urology

A. Specific Aims

1) To determine whether expression and regulation of *Alox5* and *blt1* by promoter methylation and polymorphism may contribute to prostate cancer disparity between African American and Caucasian men

B. Studies and Results

1. We have performed immunohistochemical staining of 5-lipoxygenase (5-Lox) on paraffin sections of 150 cases of African American prostate cancer and 150 cases of Caucasian American prostate cancer. Histopathological analysis is still ongoing. We plan to semi-quantify the staining intensity and compare samples of African Americans and Caucasian Americans. The purpose is to find out whether there is any significance difference in the expression of 5-Lox between African American and Caucasian American prostate cancer.
2. Using two human prostate cancer cell lines (LNCaP, PC3) and two human normal prostate epithelial cell lines (PrEC1 and PrEC2), we examined the effect of 5-aza-2'-deoxycytidine (a DNA demethylating agent) on the expression of 5-Lox and BLT1. We have not yet reached a solid conclusion regarding the potential role of promoter methylation in regulating expression of these two genes. Further improvement of our methodology is still in process.

3. We examined expression of 5-Lox in the prostate tissues of wild-type mice and TRAMP mice. Significant overexpression of 5-Lox was observed in the mouse prostate tumor as compared with wild-type tissue. We have started to cross TRAMP mice with *Alox5* knockout mice to produce *Alox5*$^{-/-}$ TRAMP mice. The purpose is to determine whether knockout of *Alox5* may reduce tumorigenesis in TRAMP mice.

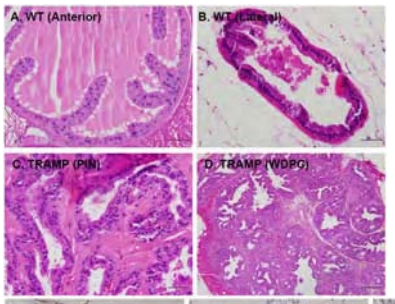


Figure 1. Histopathology of prostate tissues of wild-type and TRAMP mice.

A. anterior lobe of the prostate of the wild-type mice
B. Lateral lobe of the prostate of a wild-type mice
C. PIN lesion in the prostate of a TRAMP mice
D. Well-differentiated prostate cancer of a TRAMP mice

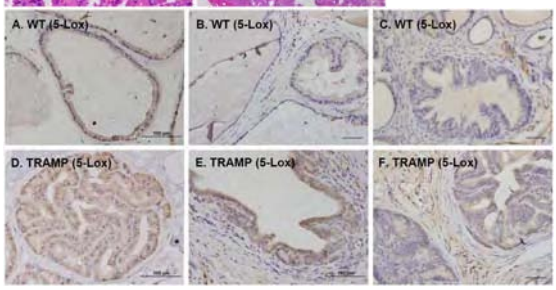


Figure 2. Expression of 5-Lox in prostate tissues of wild-type and TRAMP mice.
A, B, C: 5-Lox expression in the prostate tissues of wild-type miceD, E, F: 5-Lox expression in the prostate tissues of TRAMP mice.

C. Significance

This project is specifically designed to address one significant issue in health disparity of prostate cancer, why African American men have a higher risk of developing prostate cancer and poorer clinical outcome than Caucasian American men.

D. Plans

To continue to work on the histopathological analysis of African American and Caucasian American prostate cancer samples.

1. To improve our current methods of methylation analysis.
2. To breed *Alox5*$^{-/-}$ TRAMP mice

E. Human Subjects: protocol under revision

F. Vertebrate Animals: No change

G. Publication: No

Pilot Project #4: Anandamide-mediated Regulation of Prostate Cancer Cell Proliferation and Angiogenesis in African Americans

Investigator: Somnath Mukhopadhyay, PhD, NCCU/BBRI
Collaborator: Judd Moul, MD, Duke/Urology

A. Specific Aims

1) To define the role of CB_1 and CB_2 cannabinoid receptors in endocannabinoid methanandamide-mediated cell proliferation and androgen receptor expression in EA006AA African American prostate cancer cells.

2) Characterization of anandamide-mediated regulation of MMP activity in E006AA prostate cancer cells.

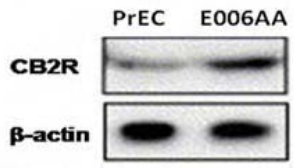


Fig. 1. Western Blot analysis of CB2R expression in PrEC and E006AA cell lysate (30 μg)

B. Studies and Results

1. Using both, RT-PCR and Western blotting we have shown (Fig.1)that in African American prostate cancer cell line (E006AA) the level of CB2 receptor (CB2R) expression is higher than normal prostate epithelial cells (PrEC).

2. We then investigated the effect of CB2 receptor (CB2R) activation on E006AA cell proliferation (Fig.2). It was found that CB2 receptor agonist JWH 133 treatment for 24 hours did not produced any significant changes in cell proliferation of E006AA cells but significantly decreased cell proliferation at 48 hours in a dose-dependent manner. We also found that CB2R antagonist (SR144528) attenuated JWH133-induced decrease in E006AA cell proliferation.

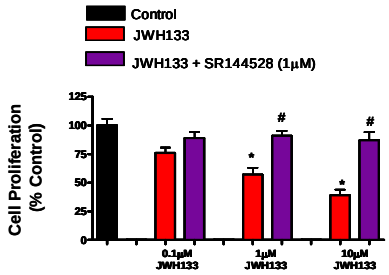


Fig.2. Effect of CB2R activation on E006AA cell proliferation

3. We have also determined that CB2 receptor activation did not alter cell viability of E006AA cells at 24 hours. We are now testing the effect of longer exposure of CB2 receptor agonist JWH 133 on E006AA cell viability. We will next determine the effect of CB2 receptor activation on androgen receptor expression.

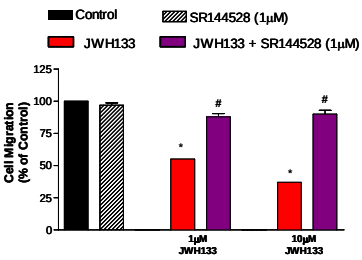


Fig.3. Cell migration was assessed by modified Boyden Chamber assay. Effect of CB2R agonist in the presence or absence of CB2R antagonist was expressed (mean ± sem from 3 separate experiments with similar results) with respect to control (% control).

Next, we will investigate the effect other CB2 receptor agonists (JWH015, CP55940 and methanandamide) on E006AA cell proliferation and cell viability. We will also determine the relative potency and efficacy of CB2 receptor agonists on E006AA cell proliferation and viability.

4. Consistent with our hypothesis, it was found that CB2 receptor activation significantly decreased cell migration in E006AA cells (Fig.3). We have also determined that CB2R antagonist SR144528 blocked JWH133-induced cell migration in E006AA cells

In coming years we will continue to investigate molecular mechanism of this response in relation to focal adhesion kinase and matrix metalloprotease activity in E006AA cells.

C. Significance

This project is addressing an important issue in health disparity of prostate cancer and results from this study will be helpful to understand the mechanism of the regulation of prostate cancer growth and metastasis in African American men population. Thus the outcome of this project has a direct therapeutic potential in terms of identifying novel drug target in the regulation of prostate cancer in African-American patients.

D. Plans

1. To obtain a detailed pharmacological characterization of CB2 receptor-mediated regulation of E006AA cells. We will determine pharmacological efficacy of CB2 receptor agonist in the E006AA African American prostate cancer cell proliferation and viability.

2. We will determine the effect of CB2 receptor activation on cell migration and metastasis using *in vitro* cell culture model.

3. We will also determine the molecular signaling mechanism of CB2 receptor-mediated regulation of FAK and MMP activity in relation to cell migration and metastasis.

E. Human Subjects: Not applicable

F. Vertebrate Animals: Not applicable change

G. Publication: No

Pilot Project #5: Feasibility of Endurance Exercise Training on Cardiovascular Risk Factors Following Radical Prostatectomy among Men with Localized Prostate Cancer: A Community-Based Intervention

Investigators: Dave Tulis Ph.D., NCCU/BBRI

Collaborators: Catherine Hoyo, PhD; Lee Jones, PhD; Stephen Freeland, MD, Duke/Urology

A. Specific Aims

1) To determine the effects of home-based endurance exercise training on exercise capacity following radical prostatectomy among with men with localized prostate cancer.
2) To assess the changes in other markers of CVD (i.e., lipid profile, blood pressure, fasting insulin, C-reactive protein, and weight status).
3) To explore the potential differential effects of exercise training between white and black American prostate cancer patients on specific aims 1 and 2.

B. Studies and Results

The following section describes the research accomplishments achieved to date associated with each tasks outlined in the approved statement of work.

1. Prepare questionnaire for exercise training

A comprehensive questionnaire was developed to assess the lifestyle and psychosocial determinants of exercise in prostate cancer patients (Appendix #1). This questionnaire was developed following an extensive literature review of pertinent work. Given that we are assessing the effects on endurance exercise training using a home-based exercise training program, it is critically important to assess the potential facilitators and barriers to exercise in this setting. Such information is critical to inform the design of future studies to maximize study adherence and intervention efficacy as well as minimize study attrition.

2. Gain Human Ethnical Approval

At Duke University Medical Center, there is a two-tiered system to obtain ethical approval to conduct clinical investigations among individuals diagnosed with cancer. Prior to submission

to the Institutional Regulatory Board (IRB), all clinical protocols have to be submitted and approved by the Duke Comprehensive Cancer Center (DCCC) Cancer Protocol Committee (CPC). Attainment of human ethical approval for the present investigation was a long and complex process. We initially submitted all materials for IRB approval on August 10th, 2007. We gained CPC approval on October 5th, 2007. We applied for full IRB review on October 8th, 2007 and finally received approved on February 27th, 2008. Based on the date of full study execution and our 'statement of work', full human ethical approval was anticipated by August 1, 2007. However, full approval was not obtained until February 27th, 2008, ~7 months behind schedule.

3. Recruitment of Patients

Since gaining IRB approval we have, unfortunately, experienced further delays. Dr. Oates (the Postdoctoral Fellow at NCCU working with the researchers at Duke) has left the program which has significantly affected our ability to recruit patients and proceed with this study. Nevertheless, we are currently actively attempting to resolve this issue and are confident that we will able to proceed with patient recruitment in a timely fashion.

C.Plans:

1. Establish an immediate plan to initiate with subject recruitment
2. Proceed with study procedures
3. Analyze and interpret data
4. Submit publication

D. Publication: No

Task #4: Training Determine the effects of home-based endurance exercise training on exercise capacity following radical prostatectomy among with men with localized prostate cancer.

a) A questionnaire for exercise training has been generated. (see Appendix #1)

b) The IRB protocol has been approved in February 27, 2008.

c) As mentioned early, since gaining IRB approval, Dr. Oates the Postdoctoral Fellow at NCCU working with the researchers at Duke has left the program to accept a faculty position at Tennessee State University (TSU). In addition, Dr. David Tulis (NCCU PI) who was working on the exercise project with Dr. Lee Jones (Duke PI), has recently accepted a position at East Carolina State University (ECU). Since the funds are not enough to hire a new postdoctoral fellow or to support a new faculty, we are working with the Duke team to modify this project.

Key Research Accomplishments:

-We have created the Collaborative Prostate Center and Develop Plan for **Training**, **Research**, and **Community Dialogue and Outreach** and have established a program advisory committee.

-We have hired and trained a Research Associate, Ms. Kelly Anderson.

-Dr. Grant and Dr. Schildkraut teamed up to write a successful training proposal for Dr. Grant entitled: “Association of the UGT2B17 Gene Deletion Polymorphism and the Incidence of Ovarian Cancer and Ethnicity”.

-Drs. Richardson, Chen and Grant in collaboration with our Duke partners wrote a successful proposal entitled: “Roles of Inflammation and Androgen Metabolism in Prostate Cancer Disparity” that was submitted in our EXPORT center grant.

-In collaboration with our partners at Duke Comprehensive Cancer Center (DCCC) and UNC Lineberger Comprehensive Cancer Center (LCCC) we have submitted a U54 grant application (U54CA137837) to the National Cancer Institute entitled “NCCU-DCCC-LCCC Partnership in Cancer Research”.

Reportable Outcomes:

1- Develop a mouse model of prostate cancer deficient in βarrestin 2 (TRAMP-$\beta arr2^{-/-}$) or 5-Lox (TRAMP-$Alox5^{-/-}$). This mouse model is important for the studies proposed in pilot projects #2 and #3.

2- Demonstrate that βarr1, not βarr2, is over-expressed in prostate cancer cells.

3- Develop SiRNA knockdown E006AA cell (SiCB2-E006AA) to study the role of CB2 receptor in these cells.

4- Establish for the first time that CB2 receptor plays a role in the regulation of prostate cancer cell proliferation and viability.

Conclusion:

Our progress for the first year of the funding period of the NCCU-Duke Collaborative Center in Prostate Cancer has been remarkable. We have accomplished the majority of the goals proposed in our statement of work for that period. Two major drawbacks have hampered our progress: a) the delay in the approval of the final IRB that has greatly impact the recruitment of subject and accrual of prostatic tissue; and 2) the early departure of Dr. Veronica Oates and now Dr. David Tulis from NCCU. Both scientists were involved in pilot project 5. The IRB is being amended based on the USAMRMC’s recommendations. We are also in the process of recruiting a postdoctoral fellow or a Research Scientist with a population-based research background to work with Dr. Jones at Duke. Due to the tight budget of the grant, we are being forced to seek funding elsewhere to accomplish pilot project #5.

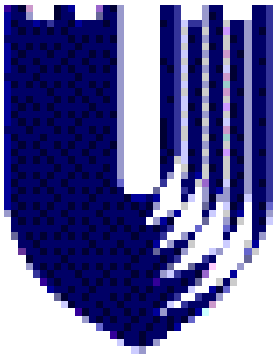
References

1. De Marzo, AM; Platz, EA; Sutcliffe, S; Xu, J.; Grönberg, H., Drake, CG; Nakai, Y.; William B. Isaacs, WB & Nelson, WG. Inflammation in prostate carcinogenesis (2007) *Nature Reviews Cancer*, 7:256-269.
2. Chen, FL; Amstrong, AJ & George, DJ. Cell Signaling Modifiers in Prostate Cancer (2008). *Cancer J.* 14:40-45.
3. Moul, J. W., Sesterhenn, I. A., Connelly, R.R., Douglas, T., Srivastava, S., Mostofi, F. K. and McLeod, D.G. Prostate-specific antigen values at the time of prostate cancer diagnosis in African-American men (1995) JAMA 274: 1277-1281

Appendices

Appendix 1:

Lifestyle Behavior Baseline Questionnaire



Duke Comprehensive Cancer Center
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Section 1: Directions

Thank you for agreeing to participate in this study. In this questionnaire, we are going to ask you a series of questions about yourself. There are no right or wrong answers. All we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 20-30 minutes to complete. All responses are completely confidential and will never be used in any way that could link them to you. It is important to complete all questions so that we can include your responses in our analyses.

For further information or if you have any questions about completing the questionnaires, please contact Miranda West, (Project Coordinator) at (919) 681-5494

After completing your questionnaire, please bring it with you to your scheduled physical fitness assessment. Keep one copy of the informed consent for your records. Many thanks in advance for considering our study.

8.7.2007

Section 2: Quality of Life

Below is a list of statements that other people with prostate cancer have said are important to their quality of life. Please indicate the extent to which you have experienced each of the following statements during the past 7 days by circling the appropriate number using the following scale.

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

During the past week:

PHYSICAL WELL-BEING

1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4

SOCIAL/FAMILY WELL-BEING

8. I feel close to my friends	0	1	2	3	4
9. I get emotional support from my family	0	1	2	3	4
10. I get support from my friends	0	1	2	3	4
11. My family has accepted my illness	0	1	2	3	4
12. I am satisfied with family communication about my illness	0	1	2	3	4
13. I feel close to my partner (or the person who is my main support)	0	1	2	3	4

14. I am satisfied with my sex life	0	1	2	3	4	

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

During the past week:

EMOTIONAL WELL-BEING

15. I feel sad	0	1	2	3	4	
16. I am proud of how I am coping with my illness	0	1	2	3	4	
17. I am losing hope in the fight against my illness	0	1	2	3	4	
18. I feel nervous	0	1	2	3	4	
19. I worry about dying	0	1	2	3	4	
20. I worry that my condition will get worse	0	1	2	3	4	

FUNCTIONAL WELL-BEING

21. I am able to work (include work at home)	0	1	2	3	4	
22. My work is fulfilling (include work at home)	0	1	2	3	4	
23. I am able to enjoy life	0	1	2	3	4	
24. I have accepted my illness	0	1	2	3	4	
25. I am sleeping well	0	1	2	3	4	
26. I am enjoying the things I usually do for fun	0	1	2	3	4	
27. I am content with the quality of my life right now	0	1	2	3	4	

ADDITIONAL CONCERNS

28. I am losing weight	0	1	2	3	4	
29. I have a good appetite	0	1	2	3	4	

30. I have aches and pains that bother me	0	1	2	3	4
31. I have certain areas of my body where I experience significant pain	0	1	2	3	4
32. My pain keeps me from doing things I want to do	0	1	2	3	4
33. I am satisfied with my present comfort level	0	1	2	3	4
34. I am able to feel like a man	0	1	2	3	4

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

During the past week:

35. I have trouble moving my bowels	0	1	2	3	4
36. I have difficulty urinating	0	1	2	3	4
37. I urinate more frequently than usual	0	1	2	3	4
38. My problems with urinating limit my activities	0	1	2	3	4
39. I am able to have and keep an erection	0	1	2	3	4

FATIGUE SUBSCALE

40. I feel fatigued	0	1	2	3	4
41. I feel weak all over	0	1	2	3	4
42. I feel listless (“washed out”)	0	1	2	3	4
43. I feel tired	0	1	2	3	4
44. I have trouble starting things because I am tired	0	1	2	3	4
45. I have trouble finishing things because I am tired	0	1	2	3	4
46. I have energy	0	1	2	3	4
47. I am able to do my usual activities	0	1	2	3	4
48. I need to sleep during the day	0	1	2	3	4

49. I am too tired to eat	0	1	2	3	4
50. I need help doing my usual activities	0	1	2	3	4
51. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
52. I have to limit my social activity because I am tired	0	1	2	3	4

Section 2: Physical Activity Questions

For this next question, we would like you to recall your average weekly physical activity for **TWO different periods** (**before** your prostate cancer diagnosis and **after** your diagnosis**)**. Considering a typical week (7 days) how many times on average, did you perform the following kinds of physical activity?

When answering these questions please:

- Only count exercise sessions that lasted **20** minutes or longer in duration
- Only count exercise that was done during **free** time (i.e., not occupation or housework)
- Note that the main difference between the three categories is the **intensity** of the exercise

	Physical activity **BEFORE** your prostate cancer diagnosis		Physical activity **SINCE** your prostate cancer diagnosis (approximately last 2 weeks)	
	Times Per Week	**Average Duration (mins)**	**Times Per Week**	**Average Duration (mins)**
a. **STRENUOUS PHYSICAL ACTIVITY (HEART BEATS RAPIDLY, SWEATING)** (e.g., running, aerobics classes, vigorous swimming or bicycling)	_____	_____	_____	_____
b. **MODERATE PHYSICAL ACTIVITY (NOT EXHAUSTING, LIGHT PERSPIRATION)** (e.g., fast walking, tennis, easy bicycling, easy swimming)	_____	_____	_____	_____
c. **MILD PHYSICAL ACTIVITY (MINIMAL EFFORT, NO PERSPIRATION)** (e.g., easy walking, yoga, golf)	_____	_____	_____	_____